REMARKS

This **Corrected Amendment** "C" is a corrected version of Applicant's Amendment "C" which was filed September 22, 2004. It is therefore responsive to the examiner's Office Actions of September 2, 2004 and January 7, 2005.

Examiner's Office Action of January 7, 2005

The examiner found that the applicant's Reply filed on September 22, 2004 was not fully responsive to the examiner's Office Action of Septemeber 2, 2004 because the amendments to the specification and claims were not submitted in proper format. **Corrected Amendment "C"** is Applicant's good faith effort to place the amendments in the format required under 37 CFR 1.121.

Examiner's Office Action of September 2, 2004

The examiner found that the Reply filed on July 19, 2004 was not fully responsive to the prior Office Action, because the amendments to the specification and claims were not submitted in proper format. It can be seen that the above amendments are in the format required under 37 CFR 1.121, so that applicant's Reply is now fully responsive.

Lactoferrin (LF) has a bilboate structure, with a positively charged N-terminus lobe and a negatively charged C-terminus lobe. A full length LF peptide sequence has about 600 to about 800 continuous amino acids. Human LF, in particular, is about 703 amino acids long and has a molecular weight of about 83,000 daltons.

Lactoferrin (LF) is a known antimicrobial agent. Its activity is highly dependent on its three-dimensional or tertiary structure. If the protein does not have the proper conformation, its activity is diminished or lost.

Now it has been unexpectedly found that LF can be stabilized and its antimicrobial activity increased, if the LF is immobilized by binding its N-terminus to a suitable, naturally occurring substrate. For LF to become immobilized on a substrate and, in particular on a naturally occurring substrate, the portion of the substrate which is to do the binding should carry the opposite charge, *i.e.*, carry a positive charge. The LF can be immobilized on a suitable naturally occurring substrate by mixing the LF with the naturally occurring substrate in a suitable medium, such as deionized water.

The Examiner rejected claims 102-104, 115-117, 119, 124, 127, 128, 137, 138, 142-148, 154, 157, 158, 171, 172, 176, 179, 180, 186, and 193-196 under 35 U.S.C. 102(e) as being anticipated by US 6,475,511 B2 ("Gohlke *et al.*"). Gohlke *et al.* describe compositions containing a combination of colostrum and lactoferrin in a "mucosal delivery format" ("MDF"). (Col. 6, lines 13-28.) The composition can also contain modified pectin. (Col. 6, lines 49-52.) By MDF is meant a composition, such as a lozenge, formed of *solid* components. For example, Gohlke *et al.* teach, "The individual components of the composition may be obtained from commercial sources: colostrum (which is dehydrated by standard spray-drying procedures known in the art)" (col. 9, lines 41-44). Furthermore, examples 1 - 3 describe a process for preparing the compositions where, "[E]ach of the following ingredients is placed, in *powdered* form, into a commercial mixer." The ingredients are then mixed and *cold pressed.* The *mere presence* of LF in a cold-pressed mixture with dehydrated colostrum or modified pectin would not result in the immobilization of the LF via its N-terminus. Instead, appropriate conditions must be chosen before immobilization can occur. As described in the instant application, LF is immobilized

by first mixing the LF with the naturally occurring substrate in *a suitable medium,* such as deionized water. Therefore, Gohlke *et al.* does not anticipate any of claims 102-104, 115-117, 119, 124, 127, 128, 137, 138, 142-148, 154, 157, 158, 171, 172, 176, 179, 180, 186, and 193-196, so that this ground for rejection should be withdrawn.

The examiner rejected claims 1, 2, 11, 18, 19, 28, 31, 39, 101-103, 119-124, 126-129, 131, 132, 134, 142-151, 153, 164, 171-173, 175, 186, 193-195, 197, and 200 under 35 USC §102(b) as being anticipated by or under 35 USC §103(a) as obvious in view of WO Patent Application 91/13982 ("WO Patent Application '982"). WO Patent Application '982 generally relates to human LF expressed using recombinant DNA. It discloses the use of this LF as a nutritional supplement, an antiseptic, and as a food-spoilage retardant. The LF can be compounded with certain carriers or diluents.

However, WO Patent Application '982 neither broadly teaches LF immobilized on a naturally occurring substrate via the N-terminus region of the LF, nor does it provide a specific example of such an immobilized LF. The examiner asserts that:

> "The WO Patent Application '982 teaches LF in combination with stearic acid (which is a lipid and also corresponds to Applicant's pharmaceutically acceptable carrier of claim 102) or its salts . . . Because the same components are present in the same defined dispersion, inherently the LF in the composition of the WO Patent Application '982 will be immobilized via its N-terminus . . . ."

Applicant respectfully disagrees. Stearic acid with a molecular weight of only 284.47 is not a substrate on which LF can be immobilized. That would be akin to saying that a dog was immobilized on a flea, if a flea attached itself to a dog.

Furthermore, the *mere presence* in a mixture of LF and stearic acid or any of the other naturally occurring carriers or diluents taught in WO Patent Application '982 would *not* inherently result in immobilization of the LF via its N-terminus on a substrate. The reference does not disclose or suggest any conditions under which the compounds could be mixed to achieve such immobilization. Merely compounding solid LF with a solid stearic acid carrier, such as by cold-pressing the solid ingredients, will not provide an environment suitable to cause the LF to become immobilized via its N-terminus region. Instead, appropriate conditions must be chosen before immobilization can occur. As described in the instant application, LF is immobilized by first mixing the LF with the naturally occurring substrate in *a suitable medium,* such as deionized water. Therefore, the rejection of claims 1, 2, 11, 18, 19, 28, 31, 39, 101-103, 119-124, 126-129, 131, 132, 134, 142-151, 153, 164, 171-173, 175, 186, 193-195, 197, and 200 as being anticipated by or as obvious in view of WO Patent Application '982 should be withdrawn.

The examiner rejected claims 1, 2, 5, 18, 19, 22, 31, 38, 39,101-103, 106, 115-117, 119-124, 126-129, 131-132, 134, 136, 142-151, 153, 164, 171-173, 175, 186, 193-197, and 200-202 under 35 USC § 102(b) as being anticipated by or under 35 USC § 103(a) as obvious in view of European Patent Application 753,309 (European Patent Application '309). European Patent Application '309 generally relates to the preparation of mixtures of lactoferrin and desferrioxamine methanesulphonate useful for the therapy of viral infectious diseases.

However, European Patent Application '309 neither broadly teaches LF immobilized on a naturally occurring substrate via the N-terminus region of the LF,

nor does it provide a specific example of such an immobilized LF. The examiner asserts that:

> "The European Patent Application '309 teaches compositions comprising LF and carriers such as paraffin oil and Vaseline (which are lipids), xantan gum and corn starch (which are polysaccharides), and lecithin (which is an emulsifier) . . . . Because the same components are present in the same defined dispersion, inherently the LF in the composition of the European Patent Application '309 will be immobilized by its N-terminus . . . "

Applicant respectfully disagrees. Paraffin oil and Vaseline are low molecular weight compounds, not substrates. LF could not become immobilized on such small molecules. Additionally, paraffin oil and Vaseline are hydrocarbons (not lipids) and do not carry any charge. As a result, neither paraffin oil nor Vaseline contain a region which will attach LF's positively charged N-terminus region.

Similarly, lecithin is a low molecular weight compound. LF could not become immobilized on such a small molecule.

Xanthan gum and corn starch do not carry any charges. As a result, neither xanthan gum nor corn starch contains a region which will attach LF's positively charged N-terminus region.

Furthermore the *mere presence* in a mixture of LF and any of the naturally occurring carriers taught in European Patent Application '309 would *not* inherently result in immobilization of the LF via its N-terminus on a substrate. Merely compounding LF with carrier, such as by cold-pressing solid ingredients, will not

provide an environment suitable to cause the LF to become immobilized via its N-terminus region. Instead, appropriate conditions must be chosen before immobilization can occur. As described in the instant application, LF is immobilized by first mixing the LF with the naturally occurring substrate in *a suitable medium,* such as deionized water. Therefore, the rejection of claims 1, 2, 5, 18, 19, 22, 31, 38, 39, 101-103, 106, 115-117, 119-124, 126-129, 131, 132, 134, 136, 142-151, 153, 164, 171173, 175, 186, 193-197, and 200-202 as being anticipated by or as obvious in view of European Patent Application '309 should be withdrawn.

The examiner rejected claims 1, 2, 5, 18, 19, 22, 31, 32, 38, 39, 101-103, 106, 115, 119-124, 126-129, 131-136, 142-151, 153, 162-165, 171-173, 181, 184-187, 193197, and 200-202 under 35 USC §102(b) as being anticipated by or under 35 USC §103(a) as obvious in view of European Patent Application 753,308 (European Patent Application '308). European Patent Application '308 generally relates to the use of LF for therapy of diseases caused by Gram positive pathogen microorganisms. However, European Patent Application `308 neither broadly teaches LF immobilized on a naturally occurring substrate via the N-terminus region of the LF, nor does it provide a specific example of such an immobilized LF. The examiner asserts that:

> "The European Patent Application '308 teaches compositions comprising LF and peppermint oil, gum base and corn starch (which are polysaccharides) . . . Because the same components are present in the same defined dispersion, inherently the LF in the composition of the European Patent Application '308 will be immobilized via its N-terminus . . . "

Applicant respectfully disagrees. Peppermint oil is a low molecular weight compound. LF could not become immobilized on such a small molecule.

Gum base and corn starch do not carry any charges. As a result, neither gum base nor corn starch contains a region which will attach LF's positively charged N-terminus region.

Furthermore, the *mere presence* in a mixture of LF and any of the other ingredients taught in European Patent Application '308 would not inherently result in immobilization of the LF via its N-terminus on a substrate. Merely compounding LF with another compounds, such as by cold-pressing two compounds, will not provide an environment suitable to cause the LF to become immobilized via its N-terminus region. Instead, appropriate conditions must be chosen before immobilization can occur. As described in the instant application, LF is immobilized by first mixing the LF with the naturally occurring substrate in *a suitable medium,* such as deionized water. Therefore the rejection of claims 1, 2, 5, 18, 19, 22, 31, 32, 38, 39, 101-103, 106, 115, 119-124, 126-129, 131-136, 142-151, 153, 162-165, 171-173, 181, 184-187, 193-197, and 200-202 under 35 as being anticipated by or as obvious in view of European Patent Application '308 should be withdrawn.

The examiner rejected claims 1-3, 5, 18-20, 22, 31, 32, 102-104, 106, 115, 119, 124, 137, 138, 142-150, 154, 164, and 165 under 35 USC § 102(e) as being anticipated by US Patent 6,066,469 by Kruzel *et al.* ("Kruzel *et al.*"). This patent discloses the use of LF as a nutritional supplement, an antiseptic, to treat and prevent opportunistic bacterial, viral and fungal infections, and as a food-spoilage retardant. It neither broadly teach LF immobilized on a naturally occurring substrate via the N-terminus region of the LF, nor does it provide a specific example of such an immobilized LF. The examiner asserts that:

> "Kruzel *et al.* teach nutritional supplements comprising LF in combination with adjuvants or diluents such as cellulose, starch, tragacanth, and sodium carboxymethlycellulose . . . . Because the same components are present in the same defined dispersion, inherently the LF in the nutritional supplements of Kruzel et al will be immobilized via its N-terminus . . . "

Applicant respectfully disagrees. The *mere presence* in a mixture of LF and any of the adjuvants or diluents, such the solids cellulose, starch, tragacanth, or sodium carboxymethlycellulose would *not* inherently result in immobilization of the LF via its N-terminus. Merely compounding LF with other solids, such as by cold-pressing two solids, will not provide an environment suitable to cause the LF to become immobilized via its N-terminus region. Instead, appropriate conditions must be chosen before immobilization can occur. As described in the instant application, LF is immobilized by first mixing the LF with the naturally occurring substrate *in a suitable medium,* such as deionized water.

Furthermore, cellulose and starch do not carry any charges. As a result, neither cellulose nor starch contains a region which will attach to LF's positively charged N-terminus. Therefore, the rejection of claims 1-3, 5, 18-20, 22, 31, 32, 102-104, 106, 115, 119, 124, 137, 138, 142-150, 154, 164, and 165 as being anticipated by Kruzel *et al.* should be withdrawn.

CONCLUSION

In light of the foregoing amendments and remarks, as well as the Supplemental Response and Declaration under 37 CFR 1.132 received by the Patent

and Trademark Office on August 2, 2004, it is believed that the application is in condition for allowance, so that a prompt and favorable action is respectfully requested.

Respectfully submitted,

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